

### ***Remarks***

Reconsideration of this Application is respectfully requested. Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

#### ***I. Status of the Claims***

Upon entry of the foregoing amendment, claims 41-51 are pending in the application, with 41 and 47 being the independent claims. Claims 41 and 47 are hereby amended. Claim 46 is sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 48-51 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

#### ***II. The Amendment***

Claims 41 and 47 have been amended to address the issues discussed in the interview conducted with Applicants' undersigned representative. Specifically, the terms "clostridial toxin" and "first ligand-clostridial toxin complex" have been amended to be "clostridial neurotoxin," "residual clostridial neurotoxin," and "first ligand-clostridial neurotoxin complex," as suggested by the Examiner during the interview. The phrase "clostridial toxin fragments or conjugates thereof" has been amended to be "clostridial LH<sub>N</sub>." Support for this amendment can be found, *inter alia*, at page 1, lines 28 to 32 to page 2, lines 1 to 2, and page 3, lines 18 to 22. The term "said preparation" has been amended to be "a preparation comprising clostridial LH<sub>N</sub>." Support for this amendment can be found, *inter alia*, at page 7, lines 18 to 22. Support for new claims 48-51 can be

found, *inter alia*, at page 8, lines 6 to 7 and page 9, lines 23-24 (claim 48); page 7, line 25 to page 8, line 4 (claim 49); page 9, lines 23 to 24 (claim 50); and page 10, lines 13 to 14 (claim 51). Accordingly, entry of this amendment is respectfully requested.

**III. *The Interview with the Examiner***

Applicants wish to thank Examiner Devi for the helpful and courteous interview held with Applicants' undersigned representative on October 4, 2006. The claims presented above and the following remarks reflect the issues that were discussed in the interview, and are believed to address all of the rejections.

**IV. *The Rejection of Claims 41-47 Under 35 U.S.C. § 112, First Paragraph***

At page 3 of the Office action, claims 41-47 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to convey to one skilled in the relevant art that that Applicants were in possession of the claimed invention at the time the application was filed.

First, the Examiner alleges that there is no descriptive support in the specification for the limitations "wherein said second ligand binds to the first ligand part of the first ligand clostridial toxin **and** to the clostridial toxin part of the first ligand-clostridial toxin complex" in claims 41, 46, and 47. Applicants respectfully traverse the rejection.

The second ligand does not simultaneously bind to both the first ligand part and the clostridial toxin part of the first ligand-clostridial toxin complex. It selectively binds to either the first ligand or the toxin to achieve the technical effect of removing the

leached ligand-toxin complexes from the eluate of the first affinity column. More specifically, the present claimed invention is a "two-part" toxin removal method. The first part of the method removes toxin from the clostridial toxin fragments via a first ligand, which selectively binds to the toxin, but not to the toxin derivative. The second part of the method utilizes a second affinity column with a second ligand which selectively binds the leached first ligand-toxin complexes. It would be clear to a skilled person in the art that the second ligand binds to and removes the ligand-toxin complexes either via the first ligand (e.g. Protein G) or via the toxin (e.g. zinc ions). *See* specification, page 10, lines 4 to 6 and 10 to 14, and page 7, line 25 to page 8, line 4.

Solely to expedite prosecution, and not in acquiescence to the Examiner's rejection, Applicants have amended claims 41 and 47 by deleting the phrase "wherein said second ligand binds to the first ligand part of the first ligand clostridial toxin complex and/or to the clostridial toxin part of the first ligand clostridial toxin complex." Applicants thereby respectfully request reconsideration and withdrawal of this rejection. Additionally, claim 47 has been amended to indicate an alternative option that the second ligand selectively binds to "the first ligand part" of the first ligand-clostridial toxin complex. Basis for this addition can be found in lines 4 to 6 of page 10 of the specification.

Second, the Examiner alleges that there is no descriptive support in the specification for a second ligand binding to the "clostridial toxin part of the first ligand-clostridial toxin complex." Applicants again respectfully traverse the rejection.

As discussed above, to achieve the technical effect of removing leached first ligand-toxin complexes, it is readily apparent to one skilled in the relevant art that the second ligand binds to *either* the first ligand part *or* the toxin part of the complex:

a further ligand that binds selectively to the first ligand, *or*  
binds selectively to *a complex of the first ligand with toxin.*

page 10, lines 4 to 6 (emphasis added); *see also* lines 11 to 13. Thus, if the second ligand does not bind to the first ligand part of the complex, it must bind to the toxin part of the complex.

Applicants respectfully request reconsideration and withdrawal of this rejection.

***V. The Rejection of Claims 41-47 Under 35 U.S.C. § 112, Second Paragraph***

At page 4 of the Office action, claims 41-47 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite and failing to point out and claim the subject matter of the invention. First, under section 9(a), the Examiner alleges that the limitation "fragments or conjugates" is vague and indefinite. Applicants respectfully traverse the rejection.

The term "clostridial toxin fragments or conjugates" refers to a fragment of clostridial neurotoxins in which the binding capability of the H<sub>c</sub> (carboxy-terminal region of the heavy chain component of the dichain neurotoxin molecule) has been deleted, but the important translocation properties of the H<sub>N</sub> domain are retained (LH<sub>N</sub>). *See* page 1, lines 28 to 32 to page 2, lines 1 to 2, and page 3, lines 18 to 22. Accordingly, solely to expedite prosecution, and not in acquiescence to the Examiner's rejection, the term "clostridial LH<sub>N</sub>" has been substituted for the term "clostridial toxin fragments or conjugates."

Second, under sections 9(b) and 9(c), the Examiner states that the terms "conjugates thereof" and "clostridial toxin fragments or conjugates thereof" lack proper antecedent basis in claim 41. The amendment renders these rejections moot.

Third, under section 9(d), the Examiner alleges that claim 41 is vague and indefinite because it is unclear how the "same 'said second ligand'" can bind to the "first ligand-clostridial toxin complex, the first ligand part of the first ligand-clostridial toxin complex, and the clostridial toxin part of the first ligand-clostridial toxin complex." Applicants respectfully traverse the rejection. As discussed on pages 6-7, the second ligand selectively binds to the first ligand-clostridial toxin complex, either via the first ligand part or toxin part of the complex. Thus, this single second ligand has binding specificity for either the first ligand or the toxin. Nevertheless, the phrase "wherein said second ligand binds to the first ligand part . . . first ligand clostridial toxin complex" in claim 41 has been deleted for the sole purpose of expediting prosecution and not in acquiescence to the Examiner's rejection.

Fourth, claim 46 has been cancelled, thus rendering moot the rejection of this claim under sections 9(e), (f), and (g).

Similar to claim 41, the limitation "wherein said second ligand binds to the first ligand. . . first ligand clostridial toxin complex" has been deleted in claim 47. The phrase "the first ligand part of" has been added to recite an alternative option that the second ligand selectively binds to the first ligand part of the first ligand-clostridial toxin complex. *See* page 10, lines 4 to 5.

Fifth, the word "the" has been added to the term "clostridial LH<sub>N</sub>" for proper antecedent basis in claim 47, as suggested by the Examiner under section 9(h).

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Finally, in light of the new amendments made to claim 41, Applicants respectfully request reconsideration and withdrawal of rejections of dependent claims 42-45 under section 9(i).

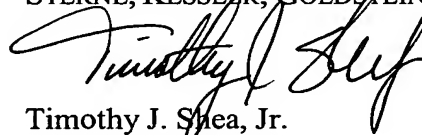
***Conclusion***

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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